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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,274	12/19/2001	David N. Herndon	D6197D	5877

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EXAMINER	
MARVICH, MARIA	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/025,274	HERNDON ET AL.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-43* is/are pending in the application.

4a) Of the above claim(s) *25-34 and 39-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-38 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Any rejection of record in the previous action not addressed in this office action is withdrawn. The new grounds of rejection herein were necessitated by amendment and, therefore, this action is final.

Election/Restrictions

Newly amended claims 25-34 and 39-42 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 25-34 and 39-42 are drawn to an invention distinct from the elected invention. Whereas the elected invention is drawn to a method of treating a wound using a cholesterol containing liposomes and a gene encoding a growth factor, the inventions of claims 25-34 and 39-42 is drawn to a method of treating a hypermetabolic effect by administration of a cholesterol containing cationic liposome and wound coverage material. The inventions are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the method of claims 35-39 and 43 do not require use of human fetal amniotic or chorionic membrane used in the instant invention as wound coverage material. The subcombination has separate utility such as for treatment of burns or other injuries without use of nucleic acid encoding the growth factors. As well a search of the combination and subcombination presents a search burden, as the combination comprises additional process steps not comprised by the subcombination, a finding that the combination, as a whole, is free of the art does not evidence patentability of the subcombination. Because the combination is narrower

in scope, a search of the combination would not adequately encompass the subcombination. Therefore, even if the subcombination were found to be free of the art, an additional search would have to be conducted to determine patentability of the combination.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 25-34 and 39-42 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Inventorship

In view of the papers filed, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by addition of Marc G. Jeschke.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 43 is rejected under 35 U.S.C 103(a) are rejected under 35 U.S.C. 103 as being unpatentable over Coffee (US Pat No. 6,252,129; see entire document) taken with McDonald et al. (US Pat No. 6,120,799) or Yang et al (Neuroreport, Vol 8, pages 2355-2358, 1997; see entire document). **This rejection is maintained for reasons of record in the office action mailed 5/22/06 and restated below. The rejection has been extended to newly added claim 43.**

Applicants' claims are drawn to methods of treating hypermetabolic response in an individual suffering a thermal injury with liposome comprising cholesterol comprising nucleic acid encoding growth factor and wound coverage material.

Coffee teaches application of a wound covering material to thermal injuries in which the matrix delivers growth factors such as fibroblast growth factor, transforming growth factor or epithelial growth factor (see e.g. col 2, line 39-47 and col 3, line 24-41) and DNA. While the growth factors are not explicitly disclosed as DNA encoding the growth factors, it would be apparent to one of ordinary skill in the art that gene delivery of the growth factors is within the scope of the teachings of Coffee et al as Coffee teaches that DNA can be used in his method, and that DNA is known to encode for growth factors and in this form is used routinely in the prior

art for expression of growth factors in target cells.. Coffee et al teach that the DNA is encapsulated in liposomes or lipids (bridging paragraph, col 3-4). While the material of Coffee is a wound-covering agent all in its own, the specification contemplates complexing the composition with conventional bandages or dressings (see e.g. col 3, line 50-54). The instant specification teaches that early wound closure decreases the hypermetabolic response, which is inherently loss of lean body mass and compromised immune response. Hence, by closure of the wound by the method of Coffee for treating burn injuries, the hypermetabolic response would be treated as recited.

Coffee does not teach that the lipid is cholesterol containing cationic liposome as a carrier or vector for the growth factor encoded DNA.

However, at the time the invention was made, McDonald et al. (column 2 bridging column 3, column 3 bridging column 4, columns 11, 16 and 17) and Yang et al. (page 2355, col 1) are exemplified references that teach that a therapeutically effective amount of a cholesterol containing cationic liposome is routinely employed in the art as carriers of growth factor encoded DNA so as to enhance gene expression of the delivered DNA in target cells of an external wound, see column 3 bridging column 4, column 12, lines 10-65, column 16 bridging column 17, column 19, last full paragraph, column 20, last paragraph bridging column 21.

It would have been obvious for one of ordinary skill in the art to have employed cholesterol-containing cationic liposomes as carriers or vectors of the DNA of Coffee so as to enhance the wound healing process of an external wound (bone rupture, ligament wound, thermal wound, or external wounds as a result of any trauma known in the prior art) in an individual. One of ordinary skill in the art would have been motivated to have employed the

liposomes employed in the cited references because McDonald et al and Yang et al are two of many prior arts of record, which teaches that cholesterol-containing cationic liposomes are routinely employed in the art as effective carriers of therapeutic materials or wound enhancing growth factor encoding gene construct to enhance an efficacy of gene expression of the gene construct at its target site.

Claims 35-38 rejected under 35 U.S.C. 103(a) as being unpatentable over Coffee (US Pat No. 6,252,129; see entire document) taken with McDonald et al. (US Pat No. 6,120,799) or Yang et al (Neuroreport, Vol 8, pages 2355-2358, 1997; see entire document) as applied to claim 43 above, and further in view of Burgess et al (US Pat NO. 6,559,119; see entire document).

Applicants' claims are drawn to methods of treating hypermetabolic response in an individual suffering a thermal injury with liposome comprising cholesterol comprising nucleic acid encoding growth factor and wound coverage material. The growth factors insulin growth factor, keratinocyte growth factor or growth hormone in the method of wound covering of thermal injuries.

The teachings of Coffee et al, McDonald et al and Yang et al are as above. However, the combination of the cited references does not teach use of insulin growth factor, keratinocyte growth factor or growth hormone in the method of wound covering of thermal injuries.

Burgess et al teach that a variety of growth factors are essential for wound healing such as from burns and teach administration of insulin growth factor, keratinocyte growth factor or growth hormone to wounds such as burns (see e.g. col 11, line 23-57, col 26, line 36-45 and col 71 line 25-36). Burgess teaches that when a tissue is injured, polypeptide growth factors are

released into the wound where they play a crucial role for healing (see e.g. col 2, line 1-16 and col 8, line 13-29).

It would also have been obvious for one of ordinary skill in the art to have further incorporate insulin growth factor, keratinocyte growth factor or growth hormone into the liposomal composition wound dressings and/or wound closure material as described in the cited references in order to enhance the wound healing process in any individual having an external wound. One of ordinary skill in the art would have been motivated to have employed growth factors because of the advantages as disclosed in Burgess et al, and because Coffee teaches that an enhancement of wound healing processes can be generated using a wound coverage material comprising therapeutic DNA. One of ordinary skill in the art would have a reasons expectation of success to practice the claimed invention particularly in view of the working examples and/or disclosures of the combined cited references, and given the state of the art as a whole, as exemplified by the combined cited references.

Thus, the claimed invention as a whole was *prima facie* obvious.

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 103 on pages 4-6 of the amendment filed 11/22/06. Applicants' argue that the methods of the cited references do not teach their use in attenuating hypermetabolic response and as demonstrated by Jeschke et al this is an unexpected systemic affect achieved when cationic cholesterol containing liposomes are administered locally to a wound site.

Applicant's arguments with respect to claims 35-39 and 43 rejected under 35 USC 103 have been considered but are not persuasive for the following reasons. The treatment of the hypermetabolic effect is a secondary result from application of the treatment to a burn injury. The MPEP teaches, 2105, "the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable." The ability of cholesterol liposomes comprising gene encoding growth factors have as an inherent property the ability to treat the hypermetabolic response and thus the subject matter is inherent in the prior art reference. However, this property is an inherent property of treatment with cholesterol containing liposomes comprising nucleic acid encoding growth factors. 2105 II, "There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference." Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Absent evidence to the contrary, the methods of the claimed invention are the same as those recited in Coffee et al in view of McDonald et al or Yang et al given that both methods involve introduction of nucleic acids encoding growth factors into burn injuries in combination with liposomes wherein the liposomes are cholesterol. Given the lack of any components or methods that distinguish the instant invention from that of the prior art, a person of skill in the art would have expected both methods to perform the same function in the same manner. The

Declaration under 37 CFR 1.132 filed 11/22/06 is insufficient to overcome the rejection of claims based upon Coffee et al taken with McDonald et al or Yang et al further in view of Burgess et al. The Declaration teaches that none of the references teach the use of the cholesterol containing liposomes to treat a hypermetabolic response. For the same reasons provided above, the Declaration is insufficient to overcome the rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

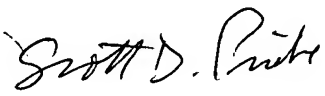
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633



SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER